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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/942,098	08/28/2001	Lance E. Steward	17451 (BOT)	6185

23601 7590 09/01/2004

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EXAMINER

MINNIFIELD, NITA M

ART UNIT	PAPER NUMBER
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1645

DATE MAILED: 09/01/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

**Application No.**

09/942,098

**Applicant(s)**

STEWART ET AL.

**Examiner**

N. M. Minnifield

**Art Unit**

1645

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 26 April 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-8,45-53,55 and 57-67 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-8,45-53,55 and 57-67 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)  | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date <u>4/26/04</u> . | 6) <input type="checkbox"/> Other: _____  |

## **DETAILED ACTION**

### ***Response to Amendment***

1. Applicants' amendment filed April 26, 2004 is acknowledged and has been entered. Claims 9-44, 54, 56 and 68-95 have been canceled. Claims 6, 45-49, 59 and 64 have been amended. Claims 1-845-53, 55 and 57-67 are now pending in the present application. All rejections have been withdrawn in view of Applicants' amendment to the claims and/or Applicants' comments with the exception of those discussed below.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

3. Claims 55 and 58 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 55 and 58 are indefinite because it contains the use of trademarks (see claims), absent sufficiently detailed descriptive generic terminology and the products denoted by trademark names are subject to change. Such trademarks, absent generic terminology, should not be used in the claims. Although trademarks accompanied by generic terminology may be used in the claims, the use of the generic terminology alone is preferred since redundancy and the use of parentheticals in the claims should be avoided.

This rejection is maintained for the reasons of record. It is noted that Applicants canceled claims 54 and 56. Further, Applicants can not be absolutely sure that these products will not change in its composition in the future.

4. Claims 57 and 59 are objected to because of the following informalities: claims 57 and 59 depend from canceled claim 54. Appropriate correction is required.

5. The provisional nonstatutory double patenting rejection of claims 1-8 and 45-67 over claims 1-6, 11, 13-15 and 31-38 of copending Application No. 10/261161 is withdrawn. It is noted that in application 10/261161, Applicants elected the methods claims, not the product claims, in response to the Restriction Requirement.

6. Claims 1-8, 45-54 and 60-67 are rejected under 35 U.S.C. 102(e) as being anticipated by Schmidt et al 6762280.

Schmidt et al discloses substrates for clostridial neurotoxins and that these substrates can be modified peptides or proteins that can serve as FRET substrates (abstract; col. 4). Schmidt et al discloses that Botulinum serotype A cleaves the protein SNAP-25 and that because botulinum neurotoxins are proteases, practical assays for this activity could form the basis for detection, quantification and drug-screening systems (col. 1). Schmidt et al discloses substrate peptides suitable for use in fluorescence resonant energy transfer assays (FRET), also known as quenched-signal assays, for the protease activities of clostridial neurotoxins (col. 3). Schmidt et al discloses "FRET substrates for proteolytic activities of clostridial neurotoxins. Each contains a fluorescent group (fluorophore) on one side of the cleavage site, and a molecule that quenches that fluorescence on the other side of the cleavage site. Upon neurotoxin-catalyzed hydrolysis, the fluorophore and quencher diffuse away from each other, and the fluorescence

signal increases in proportion to the extent of hydrolysis.” (col. 5 ; see also col. 7). The amino acid sequences set forth in pending claims 7 and 8 are in Schmidt et al (see Schmidt et al SEQ ID NO: 11 and 12). Claims 59-67 define the number of amino acid residues that the peptide of the substrate should have, and these limitations are disclosed in Schmidt et al (see SEQ ID NO: 11 and 12). The human SNAP-25 sequence is disclosed in Schmidt et al. The prior art anticipates the claimed invention.

7. Claims 55 and 57-59 are rejected under 35 U.S.C. 103(a) as being unpatentable over Schmidt et al 6762280 taken with Holskin et al 1995 (Analytical Biochemistry, 226:148-155).

Schmidt et al teaches substrates for clostridial neurotoxins and that these substrates can be modified peptides or proteins that can serve as FRET substrates (abstract; col. 4). Schmidt et al teaches that Botulinum serotype A cleaves the protein SNAP-25 and that because botulinum neurotoxins are proteases, practical assays for this activity could form the basis for detection, quantification and drug-screening systems (col. 1). Schmidt et al teaches substrate peptides suitable for use in fluorescence resonant energy transfer assays (FRET), also known as quenched-signal assays, for the protease activities of clostridial neurotoxins (col. 3). Schmidt et al teaches “FRET substrates for proteolytic activities of clostridial neurotoxins. Each contains a fluorescent group (fluorophore) on one side of the cleavage site, and a molecule that quenches that fluorescence on the other side of the cleavage site. Upon neurotoxin-catalyzed hydrolysis, the fluorophore and quencher diffuse away from each other, and the fluorescence signal increases in proportion to the extent of hydrolysis.” (col. 5 ; see also col. 7). The amino acid

sequences set forth in pending claims 7 and 8 are in Schmidt et al (see Schmidt et al SEQ ID NO: 11 and 12). Claims 59-67 define the number of amino acid residues that the peptide of the substrate should have, and these limitations are taught in Schmidt et al (see SEQ ID NO: 11 and 12). The human SNAP-25 sequence is taught in Schmidt et al. The prior art teaches the claimed invention except for the specific fluorophores of EDANS and DABCYL.

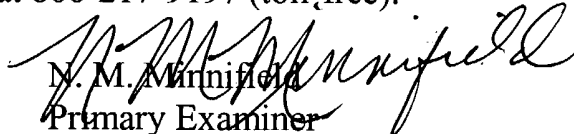
However, Holskin et al teaches substrates that comprise a donor fluorophore, acceptor fluorophore and a protease having a specific cleavage site (abstract). Holskin et al teaches the specific fluorophores of EDANS and DABCYL (abstract). Holskin et al teaches that donor and acceptor pair EDANS and DABCYL, respectively, have excellent spectral overlap properties resulting in efficient energy transfer and that strategies incorporating this donor/acceptor pair have been successfully applied to fluorescence-based assays for HIV protease, renin as well as others (p. 149, col. 1; p. 152). It would have been obvious to a person of ordinary skill in the art at the time the invention was made to combine the teachings of Schmidt et al with Holskin et al to prepare a substrate complex as taught in Schmidt et al and Holskin et al, a fluorescence-based assay, which has the donor and acceptor fluorophores and the substrate with the substrate being a clostridial toxin. Although Holskin et al does not specifically teach BoNT/A the prior art does teach this concept with several other proteins and substrates to assay for potency of therapeutic compositions and to monitor potential inhibitors. Therefore, the use of SNAP-25 and BoNT/A in a similar substrate complex would have been obvious to a person of ordinary skill in the art with the reasonable expectation of success since it had been proven successful in other substrate compositions; especially in view of the fact that Schmidt et al teaches the use of

FRET assays to monitor for therapeutic compositions or potential inhibitors. The claimed invention is prima facie obvious in view of the prior art teachings as a whole, absent any unexpected evidence to the contrary.

8. No claims are allowed.
9. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.
10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to N. M. Minnifield whose telephone number is 571-272-0860. The examiner can normally be reached on M-F (8:00-5:30) Second Friday Off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette R.F. Smith can be reached on 571-272-0864. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

  
N. M. Minnifield  
Primary Examiner  
Art Unit 1645

NMM  
August 23, 2004